REMARKS

Claims 1-79 were pending before this Response, with claims 19, and 58 being withdrawn in response to a restriction requirement. Applicants note that the Office Action (page 1) does not reflect that claims 69-79, drawn to apparatus for treating a cell proliferative disorder in a subject are pending in this case. Applicants will assume this is an oversight on the part of the Examiner, since the apparatus claims have not been cancelled by Applicants. Applicants would like to clarify that claims 69-79 read on the elected species of Group 2 (See Response to Restriction Requirement filed November 21, 2001).

By the present communication, claims 1, 24, 34, 63 and 69 have been amended. Non-elected claims 19, and 58 have also been cancelled. Claims 1-18, 20-57, and 59-79 are currently pending and under consideration in this application. The Office Action indicates (page 5) that claims 25-31 and 64-68 are considered "allowable" but are objected to based on their dependence upon a rejected claim.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 24 was rejected for allegedly being indefinite under 35 U.S.C. § 112, Second Paragraph, for failure to provide the measurement unit for the temperature range recited therein. Claim 24 has been amended merely to clarify the temperature range as being measured in degrees Centigrade. Accordingly, Applicants respectfully submit that claim 24 as newly amended meets all requirements under 35 U.S.C. § 112, Second Paragraph.

The Rejection under 35 U.S.C. § 102(e)

Applicants respectfully traverse the rejection of claims 1, 13-18, 32-33, 36-37, 52-54 and 56-57 under 35 U.S.C. § 102(e) in view of Haselton III et al. (U.S. Patent No. 6,242,258; hereinafter "Haselton"). Applicants submit that the invention methods for inhibiting cell growth or enhancing cell death, as defined by amended claim 1, and for treating a cell proliferative disorder, as defined by amended claim 36, distinguish over Haselton by including the element of "photoactivating wavelength" to the cell to achieve the claimed effect. The specification (page 1, lines 12-19) provides adequate written description for the terms "photoactivation" and "photosensitization" as follows:

> Photoactivation or Photosensitization is a process in which a photosensitive substance activated or excited by energy provided by light or heat forms a highly reactive molecule that transfers its energy (*e.g.*, hydrogen or electron) to other molecules during its return to the unactivated or unexcited state (decay). Transfer of hydrogen or electron to oxygen can form free radical or singlet oxygen, for example, as well as reactive decay intermediates, which subsequently react with or otherwise modify other components. Photooxidizing agents are a particular type of photosensitive agent that forms reactive molecules which oxidize components, and generally function by either of two pathways ...

Thus, the terms "photosensitive agent" and "photoactivating wavelength" as used in claims 1 and 36 pertain to agents that achieve their effect on cells by forming a highly reactive molecule that transfers its energy (for example, in the form of a hydrogen or an electron) to molecules in the cells under treatment during its return to the unactivated or unexcited state.

Applicants respectfully assert that the Examiner has misinterpreted Haselton as disclosing "a method for treating that includes administering a photosensitive agent" (Office Action, page 4). Applicants submit that Haselton is absolutely silent regarding the use of a photosensitive agent as the term "photosensitive agent" is used in Applicants' specification and claims, i.e., an agent. that responds to a photoactivating wavelength of light to form a highly reactive molecule that transfers absorbed light energy to molecules in cells during decay of the agent to an unactivated or unexcited state. Haselton in contrast discloses methods using a "photolabile caging group" that attaches to a molecule to inactivate the molecule. Haselton describes the chemical process involved as follows:

> The caging group of the present invention can be any caging group which is photolabile, i.e., which undergoes a chemical reaction with a target molecule whereby the caging group covalently attaches to the target molecule (Walker et al, 1988), thereby inhibiting the biological activity of the target molecule, and which upon subsequent exposure to a radiation source (e.g., UV wavelength), undergoes a conformational change that breaks the covalent bond to the target molecule and restores the biological activity of the target molecule (e.g., nucleic acid, amino acid sequence).

(Haselton, col. 4, lines 25-34). Thus the light source disclosed by Haselton is used to release the active agent from a molecule that functions much as a prodrug. Inherent bioactivity to the "caged" active agent is restored by breaking a covalent bond so that the inherent activity of the agent can be realized. Thus, the agent administered in the Haselton method is not itself "photoactive" or "photosensitive" as these terms are used in Applicants' specification and claims. That is, the caged molecule in Haselton's method does not form a highly reactive molecule by transiently absorbing energy obtained from

an irradiation source and then transfers its transiently absorbed energy (*e.g.*, in the form of a released hydrogen or electron) to other molecules (i.e., in cells) during its return to an unactivated or unexcited state.

Applicants respectfully submit that Haselton's disclosure also fails to encompass use of other types of photosensitive agents that form reactive molecules that inhibit or destroy cells by transferring energy temporarily conferred upon such molecules by an irradiating light source to adjacent cells (i.e., cells to which the photosensitive agent has been administered).

Moreover, Applicants respectfully submit that Haselton does not describe in vivo electroporation of cells in a subject to which a photosensitive agent has been administered. Haselton's description of electroporation cited by the Examiner at Col 7, line 23 pertains only to ex vivo treatment of cells; whereas Applicants' claims allow for both ex vivo and in vivo treatment of cells using the claimed methods.

Accordingly, Applicants respectfully submit that Haselton fails to disclose each and every element of claims 1 and 36 (and claims 13-18, 32-33, 37, 52-54 and 56-57 dependent thereon) as would be required to support a rejection for anticipation under 35 U.S.C. 102(e). Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection under 35 U.S.C. § 103(a)

Applicants respectfully traverse the rejection of claims 2-5, 23-24, 34-35, 38-39, 41-45, and 62-63 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Haselton in view of Zewert et al., (U.S. Patent No. 5,749,847; hereinafter "Zewert"). The remarks above concerning the deficiencies of Haselton for disclosing the invention of claims 1 and 36 apply equally here. The agent disclosed for administration in the Haselton method is not itself "photoactive" or "photosensitive" as these terms are used in Applicants' specification and claims.

It is a well-settled principle of patent law that where modification of the prior art along the lines of an applicant's invention would render the prior art inoperative for its intended purpose, the prior art does not suggest the applicant's invention (In re Gordon, 221 USPQ 1125, 1127 (Fed. Cir. 1984)). Haselton's disclosure pertains to methods wherein an isolated nucleic acid is covalently linked to a photolabile caging group that reversibly prevents expression of the nucleic acid (Haselton, Col. 3, lines 12-15). Applicants submit that substitution of Applicant's photosensitive agent in Haselton's method for controlling delivery of a nucleic acid to specific locations or tissues would render Haselton's method unsuitable for its intended use. Thus, Applicants respectfully submit that Haselton does not suggest a method of electroporation assisted delivery of an agent that is energized by light to emit a destructive moiety, such as an oxygen radical or an electron, to cells in treatment thereof.

Moreover, Applicants respectfully submit that Zewert does not cure the deficiencies discussed above of Haselton for disclosing the invention methods and apparatus. The Examiner relies upon Zewert for its disclosure of, "applying multiple pulses to the cell, applying heat to the cell and treating cancer" (Office Action, page 4). However, Applicants respectfully submit that, like Haselton, Zewert is silent regarding methods of electroporation assisted delivery of a photosensitive agent (e.g., that is energized by light to emit a destructive moiety, such as an oxygen radical or an electron) to cells in treatment thereof. Rather, Zewert's disclosure concerns only methods for delivery of a nucleotide component of a composition into an organism using electroporation to transmit the composition across the stratum corneum. Thus Applicants submit that the combined disclosures of Haselton and Zewert are not sufficient to establish *prima facie* obviousness of Applicants' invention, as defined by amended claims 1, 36 and 69. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 2-5, 23-24, 34-35, 38-39, 41-45, and 62-63 under 35 U.S.C. § 103 (a).

The Allowable Subject Matter.

The Office Action indicates (page 5) that claims 25-31 and 64-68, which depend from claims 1 and 36, are considered allowable and are merely objected to for alleged dependence upon a rejected claim. In view of the amendments herein and the above remarks regarding the freedom of claims 1 and 36 from the cited art, Applicants respectfully request reconsideration and withdrawal of the objection to claims 25-31 and 64-68.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on claims 1-18, 20-57, and 59-68 are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosure: Exhibit A

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EXHIBIT A

Version with Markings to Show Changes Made

In the claims

1. (Amended) A method for inhibiting cell growth or enhancing cell death comprising:

a) providing a photosensitive agent to a cell;

b) applying an electric pulse to the cell of a sufficient strength and duration to electroporate the cell with the photosensitive agent; and

c) applying light of [an activatable] a photoactivating wavelength to the cell thereby [activating] photoactivating the agent and inhibiting cell growth or enhancing cell death.

24. (Amended) The method of claim 23, wherein the heat has a temperature of about 36 ºC to 42 [degrees] ºC.

35. (Amended) A method for treating a cell proliferative disorder in a subject comprising:

a) administering a photosensitive agent to the subject having or suspected of having a cell proliferative disorder;

b) applying an electric pulse to a cell in the subject of a sufficient strength and duration to electroporate the cell with the photosensitive agent; and

c) applying light of [an activatable] a photoactivating wavelength to the cell thereby [activating] photoactivating the agent and treating the cell proliferative disorder.

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63. (Amended) The method of claim 62, wherein the heat has a temperature of about 36 <u>°C</u> to 42 °C.

69. (Amended) An apparatus for treating a cell proliferative disorder in a subject comprising:

a) an electrode capable of applying an electric pulse of sufficient strength and duration to electroporate a cell in the subject; and

b) a light conductor for <u>externally</u> applying light of [an activating] <u>a photoactivating</u> wavelength to the electroporated cell.